Bibliometric Analysis of Studies on Tumor Organoids

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Research

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Abstract

Background: Organoid is an artificially grown mass of cells or tissues, which is similar to an organ. It can replicate the complexity of an organ and can be used for gaining a better understanding of diseases. In this study, the hot spots of “organoids” were classified into 6 categories and 10 aspects, and organoids used for studying genetic mechanisms, drug effect, and metabolism of tumors showed the greatest potential for future development.

Methods: A total of 1550 articles relevant to organoid in tumor research field were recruited as research samples. High-frequency words and text/co-word matrix were constructed by BICOMB software. gCLUTO software was applied to analyze the matrix by double-clustering and visual analysis subsequently to identify the hotspot in this area.

Results: We constructed a text and co-word matrix composed of 21 high-frequency words and 1550 articles and generated a hotspot “peak map” based on double-clustering analysis. The strategic coordinates approach was used to assess the research prospects of each hotspot and the connections between these hotspots.

Conclusions: In this study, we classified the hot-spots of “organoid” into 6 categories and 10 aspects. Calculation and analysis revealed that the field of tumor organoid shows a slight trend of polarization, and organoid for studying the genetic mechanisms, drug effects and metabolism of tumor shows the greatest potential for future development.

Introduction

The organoid is an artificially grown mass of cells or tissues in vitro, which contains multiple types of cells to mimic its corresponding in vivo organ[1]. On the one hand, an organoid is used to study the development of normal organs, including brain, kidney, adenohypophysis, cerebellum, hippocampus, stomach, lung, thyroid, small intestine, liver, prostate, and mammary gland. On the other hand, the organoid is also used to mimic the development of multiple diseases, such as infectious diseases, hereditary diseases, and tumors[2].

An organoid provides a new insight for understanding the disease, particularly in the field of tumors. It can simulate a more physiological human cancer model in vitro, and hence can translate research from benchside to bedside more efficiently[3]. The area of tumor organoids has gained the attention of many researchers owing to the aforementioned advantages and emerging challenges in the field of tumors [4]. Subsequently, a large number of studies were performed on different aspects of tumor organoids. These studies provided vital information on the variation trend of findings on tumor organoids. This trend helped newcomers and current researchers to choose their research topics. However, analyses of studies on tumor organoids were few.

In this study, a bibliometric analysis was performed by co-word analysis and visualization on tumor organoids. The study described related findings on tumor organoids and their current trend. The hot spots in tumor organoids were analyzed, and the distribution of relevant studies based on tumor type was shown to understand the field of tumor organoids better. This information helped researchers choose research topics, design research projects, and estimate research values.

Materials And Methods

Related studies were obtained from the PubMed database. The advanced search function was used to limit research topics. The detailed search statement was as follows: ((neoplasm [MeSH Major Topic]) AND organoid). This search yielded 1550 relevant study, which were defined as the literature set. All records were preserved in the XML format.

Data extraction and analysis

Data extraction and matrix construction were performed using co-occurrence matrix generation software (BICOMB), which was developed by Professor Lei Cui from China Medical University[5]. The findings relevant to tumor organoids were examined, and the most frequent major Medical Subject Heading (MeSH) terms were counted from the literature set (Table 1). Then, a binary matrix was produced from the literature set using BICOMB. A row was set by identifying studies with their PubMed-Indexed for MEDLINE (PMID), and a column was set as MeSH terms (Table 2). Afterward, gCLUTO 1.0 software (developed by Rasmussen, Newman, and Karypis at the University of Minnesota) was applicated[6].

Table 1
High-frequency major topic word from the included publications on organoid (n = 1550).

No.	Topic word	Frequency n (%)		Cumulative percentage, %
1	Skin Neoplasms / pathology	76	1.2745	1.2745
2	Organoids	63	1.0565	2.3310
3	Organoids / ultrastructure	58	0.9727	3.3037
4	Organoids / pathology	54	0.9056	4.2093
5	Breast Neoplasms / pathology	50	0.8385	5.0478
6	Organoids / drug effects	38	0.6373	5.6851
7	Adenocarcinoma / pathology	34	0.5702	6.2552
8	Antineoplastic Agents / pharmacology	32	0.5366	6.7919
9	Nevus / pathology	31	0.5199	7.3118
10	Carcinoma / pathology	28	0.4696	7.7813
11	Colorectal Neoplasms / genetics	28	0.4696	8.2509
12	Lung Neoplasms / pathology	28	0.4696	8.7204
13	Pancreatic Neoplasms / pathology	27	0.4528	9.1732
14	Organoids / metabolism	25	0.4193	9.5925
15	Models, Biological	25	0.4193	10.0117
16	Adenoma / pathology	25	0.4193	10.4310
17	Neoplasms / pathology	25	0.4193	10.8502
18	Colonic Neoplasms / pathology	23	0.3857	11.2360
19	Liver Neoplasms / pathology	22	0.3689	11.6049
20	Teratoma / pathology	22	0.3689	11.9738
21	Nevus, Pigmented / pathology	22	0.3689	12.3428
22	Thymus Neoplasms / pathology	21	0.3522	12.6950
23	Breast Neoplasms / metabolism	21	0.3522	13.0471
24	Carcinoid Tumor / pathology	21	0.3522	13.3993

Table 2
High-frequency topic word terms-source articles matrix (localized).

No.	Topic Word	PubMed Unique Identifiers of source article				
		10048709	10078927	10095889	…	1057351
1	Skin Neoplasms / pathology	0	0	0	…	0
2	Organoids	0	0	0	…	0
3	Organoids / ultrastructure	0	0	0	…	0
4	Organoids / pathology	0	0	0	…	0
…	…	…	…	…	…	…
23	Breast Neoplasms / metabolism	0	0	0	…	0
24	Carcinoid Tumor / pathology	0	0	0	…	0

Strategic coordinates

The co-word analysis was used as a tool to describe the relationship between scientific topics; it helped investigate the differences between local and global environments of each research topic[7]. The co-word matrix composed of high-frequency words was used to calculate the intraclass and interclass link averages using Excel (Table 4).

Results

The search strategy yielded 1550 studies related to tumor organoids. Year-standardized studies and the corresponding organoid search index in Google are shown in Fig. 1. Also, 2773 major topic terms were extracted from the studies on PubMed. As described in the high-frequency term table (Table 1), the frequency number before the 21st word was larger than its original number, and the 22nd and 23rd words shared the same frequency number with the former one. However, after the 24th word, the ordinary number was higher. The terms ranked before the 21st word were related to 736 studies and defined as frequent terms. Then, a co-occurrence analysis of the high-frequency terms was applied. A row was set by identifying studies with their PMID number, and a column was set as MeSH terms (Table 2). In this table, “1” represented the term present and “0” represented the term absent in the reference. These references were distinguished by their PMID number. Finally, a co-word matrix was established (Table 4). This matrix indicated terms present in the selected studies, which showed the association between two topics and their accumulative number (Table 4).

The packed bubble graph was used to visualize based on PubMed so as to describe the hot topic distribution in the field of tumor organoids. In the PubMed database, the larger the weight of the topic, the larger the area, and the more central the module (Fig. 3).

Subsequently, a peak map and a double-clustering heat map were generated, and gCLUTO was used to perform data visualization based on the high-frequency terms in the literature set, which could directly detect the relationship between studies. Moreover, peak, volume, height, and color were all used to describe the associated cluster. According to the literature set, six clusters from 0 to 5 were recognized. Figure 1 shows the heat map of double-clustering visualization, where rows comprise high-frequency major MeSH terms, with the columns of corresponding terms located on the right. The bottom of the heat map showed the PubMed unique identifier of each study. A deep red grid represented a relatively higher frequency of major MeSH terms in the study, while a white grid represented a value closer to zero; negative values were green. The double-clustering matrix visualization showed that 21 highly frequent major MeSH terms were clustered in 6 peaks. In Fig. 1, the hierarchical tree on the left side denotes the relationship between high-frequency MeSH terms, while the hierarchical tree on the top denotes the relationship between studies. The highest expression of MeSH terms in each category was also examined. In Fig. 2, each category is numbered from 0 to 5. Peak, volume, height, and color were all used to provide information about the associated cluster. The peak is the specific area in each topic. The volume is the accumulative article volume in the topic. The more the papers, the higher the height. Moreover, red indicates a low deviation, and blue indicates a high deviation (Fig. 2). The detailed cluster is summarized in Table 3.

Table 3
Descriptive and discriminating features and representative articles

Descriptive and Descriminating features				
Cluster 0	Size 3	ISim: 0.794	Esim: 0.024	
Descriptive	10048709	10340047	1054896	10078927
Descriminating	10048709	10340047	1054896	1026920
Cluster 1	Size 3	ISim: 0.533	Esim: 0.025	
Descriptive	1057351	10399173	10571348	1032517
Descriminating	1057351	10399173	10571348	10048709
Cluster 2	Size 4	ISim: 0.451	Esim: 0.049	
Descriptive	1026920	10417695	10463034	10403302
Descriminating	1026920	10463034	10417695	10403302
Cluster 3	Size 4	ISim: 0.339	Esim: 0.032	
Descriptive	10323079	1032522	10095889	10483587
Descriminating	10323079	1032522	10095889	10483587
Cluster 4	Size 5	ISim: 0.335	Esim: 0.047	
Descriptive	10470114	1032517	10342010	10459830
Descriminating	10470114	10342010	10459830	1032517
Cluster 5	Size 5	ISim: 0.306	Esim: 0.032	
Descriptive	1057348	10416596	1057348	10392634
Descriminating	1057348	10416596	1057348	10392634

Table 4
A co-word matrix of high-frequency major topic (localized).

No.	Topic Words	Skin Neoplasms / pathology	Organoids	…	Carcinoid Tumor / pathology
1	Skin Neoplasms / pathology	76	2	…	0
2	Organoids	2	63	…	0
3	Organoids / ultrastructure	2	0	…	0
…	…	…	…	…	…
24	Carcinoid Tumor / pathology	0	0	…	21

In addition, the main groups and the current trend of research in the tumor organoid field was determined by investigating the studies corresponding to each category of clusters. In this way, some clusters could be subdivided or integrated into different topics:

1. Pathology for skin cancer and nevus (cluster 0)
2. Pathology for thymus cancer (cluster 1)
3. Pathology for lung carcinoma (cluster 1)
4. Pancreatic cancer organoid and biology model (cluster 2)
5. Organoid for antineoplastic agents of liver cancer (cluster 3)
6. Organoid for genetic study of colorectal carcinoma (cluster 4)
7. Organoid for metabolism study of breast cancer (cluster 4)
8. Pathology for adenocarcinoma (cluster 5)
9. Pathology for carcinoid tumor (cluster 5)
10. Pathology for teratoma (cluster 5).

Discussion

Organoids can mimic specific aspects of the 3D architecture, cell-type composition, and functionality of real organs while maintaining the advantages of simplified and easily accessible cell culture models[8]. As such, they hold great promise for a range of biological and biomedical applications. However, the related studies often focus on topics such as specific disease modeling, drug discovery, or other aspects; no macroscopic analysis or scientific prediction of tumor organoids has been conducted using bibliometrics[9–12]. In this study, the method of co-word research and double-clustering visualization analysis was used to obtain 6 categories of 10 aspects of tumor organoids as hot spots. According to the co-word matrix, hotspot strategic coordinates were constructed, and an organ or disease distribution map

was generated to understand the weight of each organ or disease in the tumor organoid field. These results suggested that the tumor model study was an absolute core topic with much interaction with the other categories and good integrality. The organ or disease profile showed that the two most important organs or diseases for tumor organoids were the skin and breast cancer. This distribution might be due to drug effects on skin and breast cancer tested using organoids [13–14]. Several tumors such as carcinoid tumors had few counts, probably because their prognosis depended on location and pathology; the main method was the surgical therapy[15]. The analysis of the extracted literature set showed that the recent tumor organoid research was dominated by disease modeling. In the study of disease modeling, the subcategory analysis indicated that the most popular topics were disease genetic mechanism, drug effect, and metabolism. Although the co-word clustering analysis of high-frequency words is a new method of analysis, a certain degree of bias may exist due to word selection among researchers when writing. Additionally, the quality of studies in the PubMed database is not uniform. Although 1550 study were examined, the dataset may be incomplete due to limitations of intelligence in the retrieval system.

Conclusions

Co-word analysis and co-citation analysis of studies on tumor organoids were performed using various scientometric tools, and 6 categories and 10 hot topics were summarized. The current state of research in this field is polarized. Further, the tumor model is at the absolute core with the most mature research on disease genetic mechanism, drug effect, and metabolism. Future bibliometric analyses should explore the exact function of tumor organoids in different kinds of tumors.

Abbreviations

MeSH: Medical Subject Headings; gCLUTO: Graphical Clustering Toolkit;

Declarations

Authors' contributions

Conceptualization: CQW, ZY: Data curation: CQW, ZY, LK Formal analysis: CQW, WY; Methodology: CQW, MGY; Writing-original draft: CQW, ZY; All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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Figures

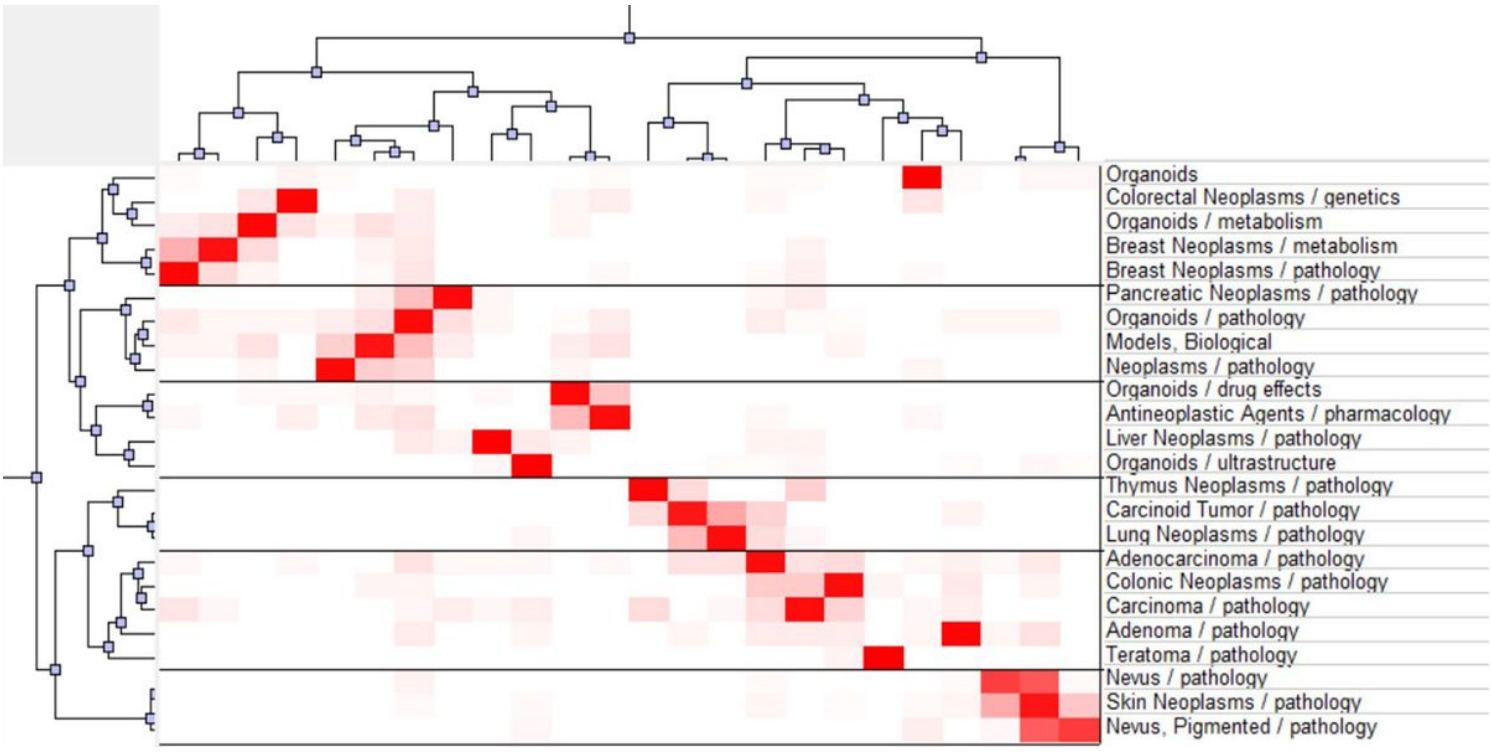

Figure 1

Visualized matrix of biclustering of highly frequent topic words and PubMed Unique Identifiers (PMIDs) of articles on tumor organoids

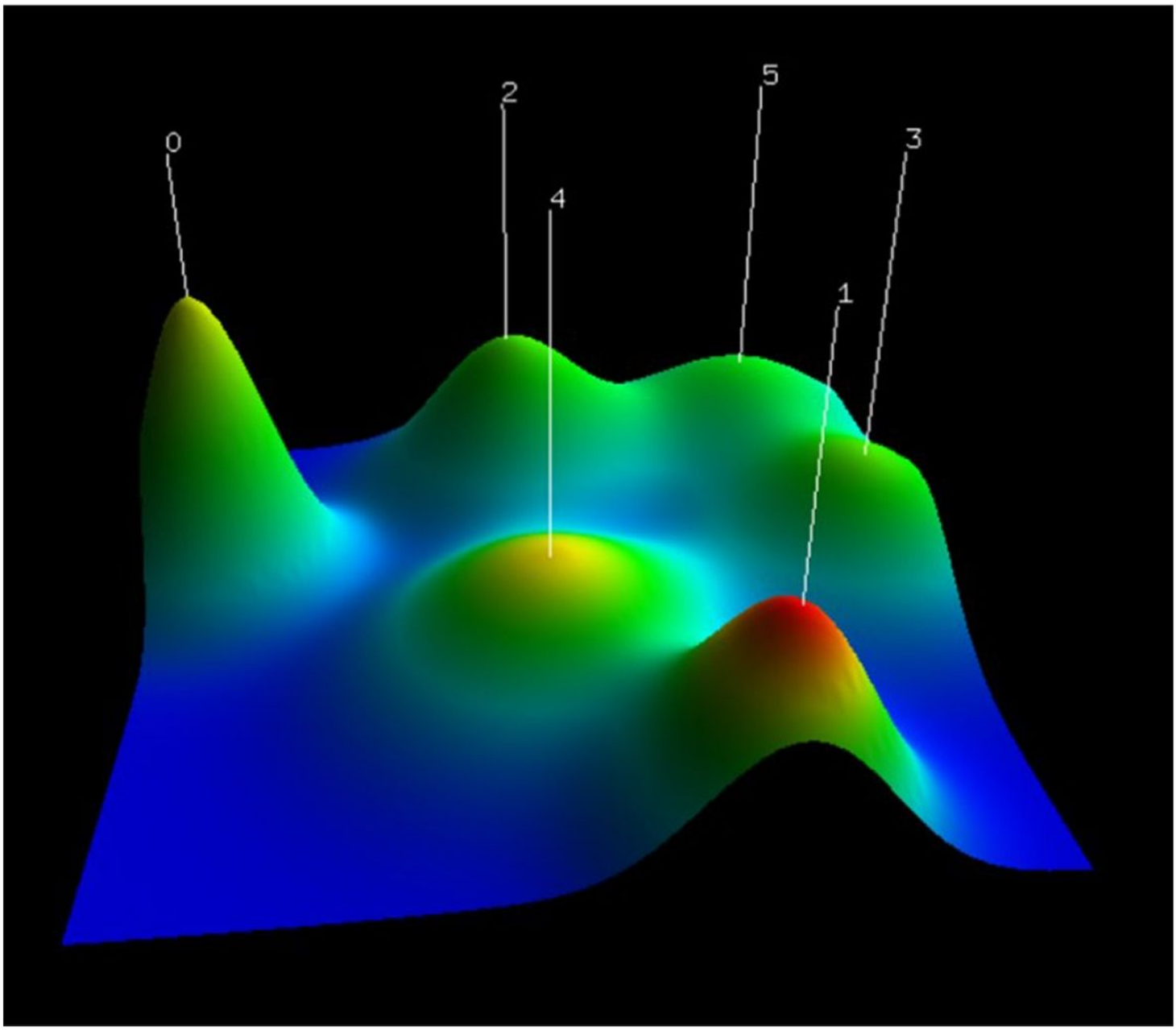

Figure 2

Mountain visualization of biclustering of highly frequent major topic words and articles on tumor organoids.

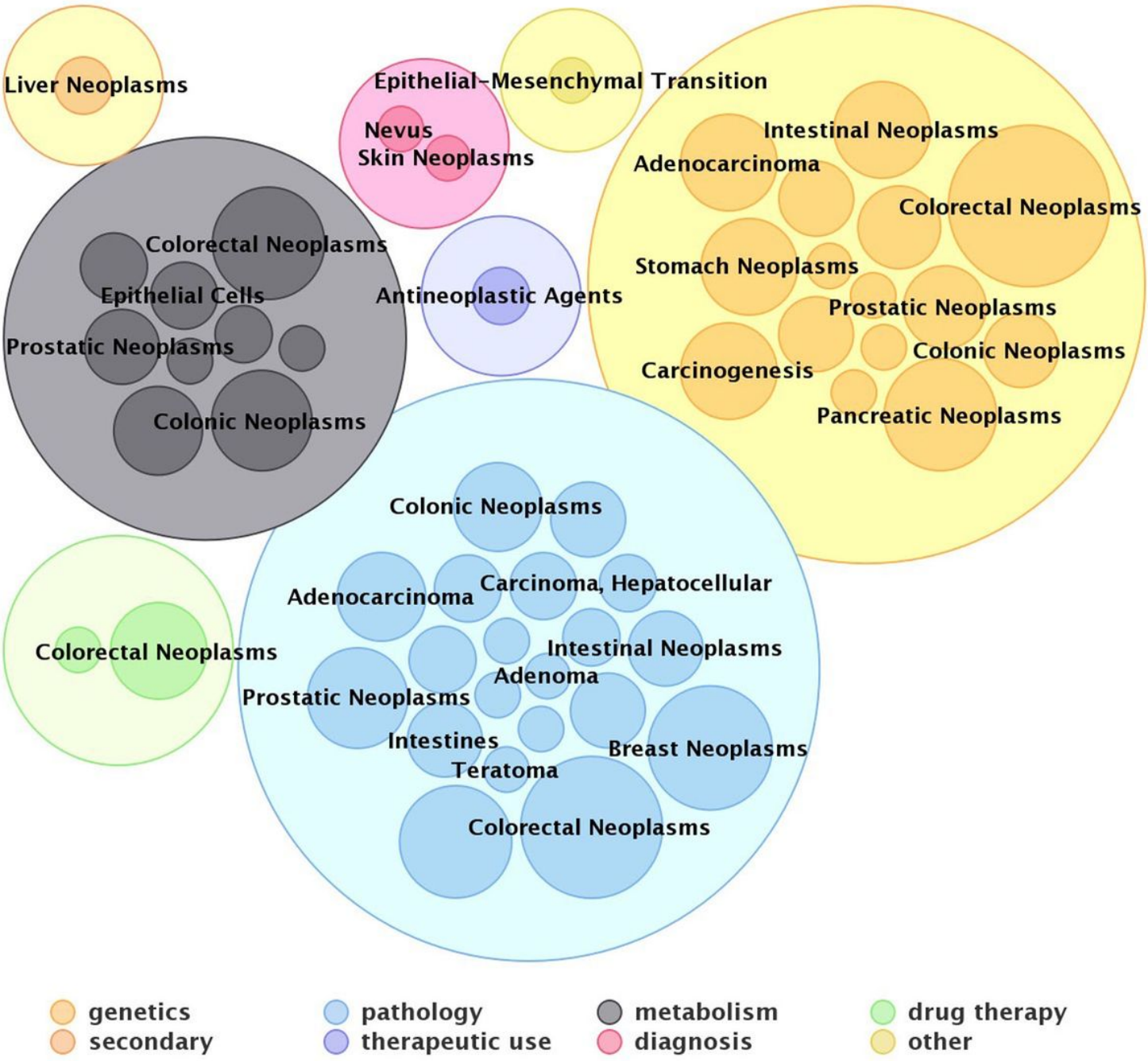

Figure 3

A survey of major topics in tumor organoid shown. The visualizations were done using the Carrot system based on the top-ranking results of search.